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A REPORT OF TWO CASES OF ACTINOMYCOSIS
OF THE BRAIN.

A REPORT OF TWO CASES OF ACTINOMYCOSIS OF THE BRAIN.

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From the Pathological Anatomical Institute of Professor Chiari in Prague.

FOR the material from these cases, as well as for much kind advice and assistance, I am indebted to Professor Chiari, in whose institute the cases were first examined and the autopsies made.

Merely a cursory glance over the total number of cases of actinomycosis in man, hitherto published, is necessary to convince one how comparatively rare are metastases in any form, the affected organs in most of such instances belonging to the thoracic and abdominal cavities. In the brain, however, metastases are peculiarly rare, and the most careful perusal of the various monographs and compilations on the disease fails to reveal more than 3, or at most 4, cases of the kind.

Ponfick,¹ in his well-known work, describes the oft-quoted case (Frau Deutschmann), in which, among other metastases, there were found, in the brain, abscesses containing the actinomyces fungus. Apart from this, however, the author had observed no case of a similar nature, though he further records an instance in which the disease, having commenced in the prevertebral region, advanced *per continuitatem* to the brain and meninges (August Barunké).

J. Israel,² who in 1885 had collected 38 cases, mentions but one other instance of actinomycotic metastases in the brain, observed and placed on record by König and O. Israel.³ Here the disease, as viewed by J. Israel, having commenced in the lungs, was propagated through blood channels to various organs of the body, involving likewise the brain and its membranes.

In this work is further cited the case observed by Zemann,⁴ and considered by him as primary actinomycosis of the Fallopian tube, with the formation of secondary abscesses in the liver, lungs, and brain.

¹ Ponfick, "Die Aktinomykose des Menschen; eine neue Infektions-krankheit." Berlin, 1882.

² J. Israel, "Klinische beiträge zur Kenntniss der Actinomykose des Menschen."

³ König and O. Israel—König, "Ein fall von Actinomycosis hominis." Inaug. Diss. Berlin, 1884. O. Israel, *Berl. klin. Wochenschr.* 1884, No. 23.

⁴ Zemann, "Ueber die Aktinomykose des Bauchfells und der Baucheingeweide beim Menschen," *Wien. med. Jahrb.* 1883.

That these abscesses, however, are to be regarded as actinomycotic is uncertain, in that the author failed to discover in any of these metastases the parasite which excited the primary lesions.

J. Israel himself had never observed any case of actinomycosis with cerebral abscesses, nor has Boström,¹ in his otherwise exhaustive and elaborate treatise on the subject, made any mention of their occurrence.

There remains, lastly, to be mentioned the interesting article by Bollinger,² describing a primary actinomycosis of the brain, in which the only discernible lesion was an actinomycoma, situated between the anterior pillars of the fornix.

Considering, then, the marked rarity of cases such as those here mentioned, and that they, moreover, present certain peculiarities which differentiate them from others, the subjoined communication may perhaps be justifiable.

CASE 1.³—W. W., æt. 38, a blacksmith; had been for some time under treatment in the klinik of Prof. Gussenbauer, on account of a phlegmonous condition of the sternum and tissues about it—of 5 months' duration. This was incised and treated in the usual manner. The patient, however, became gradually worse, presented symptoms pointing to pulmonary tuberculosis, and finally, 3 weeks after the operation, died, with evident signs of a complicating tubercular affection of the meninges.

The autopsy (performed as a class exercise, November 15th, 1886) presented the following conditions:—

The body was that of a medium-sized well-built man; emaciated; post-mortem lividity in dependent parts. Pupils somewhat contracted and equal. Thorax well developed; on the anterior surface in the region of the manubrium sterni and corpus was a large ulcerated area, 10 cm. in diameter, involving the skin and subcutaneous tissue, and extending in several places to the subjacent bone and ribs. A sinus from here communicated with the thoracic cavity. From the right border of the ulcer was an incision 10 cm. long, exhibiting, along its deepest parts, softening tissues infiltrated with pus. The lower portion of the manubrium sterni and part of the corpus were absent, a finger being thus readily admitted into the suppurating mediastinal tissue. The sternal end of the cartilage of the second rib on the left side was likewise wanting, while the corresponding cartilage on the right side was stripped of perichondrium.

The head.—Soft tissues of scalp pale. Skull of normal size and configuration. Dura mater tense, its sinuses containing fluid blood and post-mortem clot. The inner meninges pale and delicate throughout, except beneath the longitudinal sinus, where a few Pacchionian granulations were found. Moderate adhesion of the meninges to the convolutions, which latter were markedly flattened, and the whole brain swollen. Basal arteries thinned. Cerebral substance pale, soft, and oedematous. In the left occipital lobe were found three rounded abscesses, each about the size of a walnut and containing thick, green, fetid pus. These, though surrounded by a definite "pyogenic" membrane, communicated with each other and occupied almost the entire white substance of the lobe, encroaching, too, over its lateral surface to the

¹ Boström, "Untersuchungen ueber die Aktinomykose des Menschen," *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1891, bd. ix.

² Bollinger, "Ueber primäre Aktinomykose des Gehirns beim Menschen," *München, med. Wchschr.* 1887.

³ Demonstrated by Prof. Chiari, before the Verein deutscher Ärzte in Prag, Dec. 10th, 1886.

cortex. In the ventricles there was but a small quantity of serum, and elsewhere no pathological condition beyond a small localised area of intense hyperæmia on the cortex of the right middle frontal lobe.

The *pharynx*, *larynx*, and *trachea* were normal. The *teeth*, though incomplete, manifested no sign of caries; and the alveolar process, from which the lacking teeth had disappeared, showed no change other than atrophy. The *tonsils* were of normal size, their crypts containing a small quantity of mucus.

On removal of the *sternum*, not only was the area about the sinus found involved, but, further, the whole posterior surface of the manubrium sterni and corpus, as well as the sternal ends of the first three pairs of ribs, were markedly eroded, while osteophytic deposits, thickening of the pericostæum, and purulent infiltration were superadded.

The *mediastinal tissue* was very dense and purulent, and penetrated by numerous sinuses running in various directions. Nor was the phlegmonous condition confined to these limits, but could readily be traced hence to the parenchyma of both *lungs* at their apices. Here the anterior and external portions were most involved, each lung consisting at this part of a dense mass of infiltrated tissue, in size equal to an orange. Both lungs in these areas were penetrated by numerous sinuses, the condition on the left side being more advanced, and presenting cavernous dilatations amid a compact mass of pigmented cicatricial tissue. Thickening of the large interlobular septa characterised the main changes in the right lung. Apart from these conditions were delicate apical adhesions of the pleura, hyperæmia of both lungs, and a moderate grade of lobular pneumonia in the right lowest lobe. The bronchi contained mucopurulent secretion; the peribronchial lymph glands somewhat enlarged and anthracotic.

In no other organ were any definite pathological lesions to be discovered. The right *tibia* and *femur* were also examined, being sawn through in a longitudinal direction, likewise the whole *vertebral column*, but in none was there any evidence of pathological change.

Microscopic examination of *fresh specimens of the pus* removed from the abscesses in the brain and lungs, as well as from the sinuses in the skin, revealed the presence of *actinomyces* in all.

PATHOLOGICAL ANATOMICAL DIAGNOSIS.—*Actinomycosis pulmonum, sterni et costarum; abscessus actinomycotici metastatici cerebri lobi occipit. sin.; bronchitis suppurativa; Pneumonia lobularis lobi infer. dextri; cirrhosis hepatis grad. levioris.*

Specimens hardened in alcohol, embedded in celloidin and variously stained with magenta, orseille, hæmatoxylin, and eosin, were prepared from the affected portions of the lungs and pleura, brain, skin, and retrosternal tissue.

The sections from the *lungs and pleura* presented a condition of extensive and advanced chronic inflammation. Where the pleural surfaces were seen there was a marked increase of fibrous tissue, containing in some places but few long spindle-shaped nuclei, while in others the nuclei were more numerous, short and rounded, the latter apparently representing a more recent process. In such specimens the fibrous tissue was seen to be invaded by narrow tracts of suppuration, these containing large numbers of pus cells in a state of fragmentary and fatty degeneration. The walls of these sinuses consisted of dense fibrous tissue, which likewise was infiltrated with small round cells,

extending to a greater or less distance from the margin. The actinomyces, which were here both large and numerous, showed distinctly the clubbed formation of their fibrils, and were surrounded on all sides by leucocytes lying within the suppurating tracts. Dense bands of fibrous tissue, dipping down from the pleura into the lung tissue, participated in the fibroid change. The interlobular as well as the interalveolar septa were markedly thickened and beset with anthracotic pigment. In the bronchi extensive changes had likewise occurred, small round cells in various stages of degeneration filling their lumina, while in many instances there was but little evidence of epithelial lining. The walls, further, were to a marked extent the seat of purulent infiltration, which could be traced to various distances into the surrounding tissue, as well as filling the alveoli themselves. In this way suppurating tracts had evidently arisen, and according as these were cut transversely or in a longitudinal direction, different pictures would be afforded — in the former case, giving the appearance of numerous minute abscesses amid fibrous tissue, in the latter case showing definitely the sinus-like tract formed by the parasite of the disease.

Sections of the brain, at the margin of its abscesses, showed that these, for the most part, were well defined in their boundaries, their walls, though infiltrated with small round cells, making a rapid transition to the normal brain tissue. In the surrounding cerebral substance, the vessels were dilated and filled with blood, presenting, further, collections of leucocytes in the tissues around their walls, where, likewise, there was proliferation of the connective tissue elements, and swelling of the neuroglia cells. The actinomyces, which were readily demonstrated, were small, stained well, and existed chiefly, as in the lungs, amid the small round cells within the abscess cavity. Specimens from the anterior thoracic wall, cut so as to include the sinuses, showed conditions where masses of pus cells, surrounded by more or less dense fibrous tissue, were the prominent feature. In addition, a moderate amount of granulation tissue was present outside the abscess cavity amid the fibrous masses. Centrally situated among the pus cells were numerous actinomyces, which, however, stained less readily than those in the brain, where apparently the process was one of much more recent date. The retrosternal cellular tissue presented changes of a similar nature to those in the thoracic wall, though with a greater preponderance of granulation tissue surrounding the abscess cavities. As in all the other sections, so here, large numbers of small round cells were found closely surrounding the actinomyces, whose stage of development was apparently of a date approximating those found in the thoracic wall.

CASE 2.—J. K., æt. 16, a labourer; was admitted on June 2nd, 1892, to the medical klinik under the care of Professor Dr. Pribram. From the history there taken it may be mentioned that in November 1891 there was observed in this patient a chronic suppurative process, considered by him as spon-

taneous in origin, on the right leg to the inner side of the tibia. In the following March an analogous process manifested itself in the superficial structures on the right side of the thorax. Early in May, while driving in a carriage, patient experienced sudden palpitation of the heart, followed by a left hemiplegia; headache and occasional vomiting supervened. On admission the above history was confirmed by clinical observations: a left hemiplegia with left facial paralysis—several sinuses in the right leg to the inner side of the tibia, and on the right side of the thorax. Physical examination revealed dulness and bronchial breathing over the lower half of the right lung. The headache and vomiting still persisted. On June 10th bilateral optic neuritis was discovered, and on the following day, for the first time, rigidity of the neck muscles. Patient lost consciousness on the 14th, and died the next day at 6.45 P.M.

The CLINICAL DIAGNOSIS was as follows:—*Chronic cerebral tuberculosis of the right hemisphere, followed by basal tubercular meningitis (double optic neuritis); left hemiplegia; tubercular osteitis of the sixth and seventh ribs of right side; apical pulmonary tuberculosis.*

AUTOPSY (performed June 16th, 1892, 15 hours after death).—*Body* was that of a young man, 147 cm. long, of slender build; panniculus adiposus thin; lividity in dependent parts; rigor mortis present; pupils moderately dilated and equal; visible mucous membranes pale. The *teeth* were all present and in good condition, with the exception of the left inner incisor of the upper jaw, which was absent, while on the anterior surface of the mucous membrane of its alveolar process there was a small area of ulceration. A probe introduced at this point could be carried along a fistulous tract 1 cm. long and leading down to bared bone.

The *thorax*, of normal size and well developed; on the right side in the region about the anterior axillary line, from the sixth to the eighth ribs, were the openings of several sinuses into which a probe could be passed in various directions beneath the undermined skin. Behind, at a point slightly to the right of the eighth and ninth dorsal spines, was a similar opening about 2 cm. in diameter. On slitting up the sinus leading from it, the subcutaneous tissue was found to be involved over an area about 10 cm. in diameter, while in the muscles were numerous greyish-red nodules varying in size from a hempseed to a walnut, all presenting a softened centre and in many cases intercommunicating by suppurating tracts. At no point, however, was any connection with the vertebrae visible, nor could any of these sinuses be shown to communicate with those in the right side of the thorax. Numerous fibrous strands traversed these areas in various directions. To the inner side of the *right tibia*, along its upper half, were several other orifices situated amid pale violet coloured cicatricial tissue and leading beneath the skin; incision into the part showed the muscles on the inner side of the leg, from the knee downwards, beset with suppurating tracts running between bands of fibrous tissue. The *tibia* and *fibula* were found intact.

The *head*.—Skull mesocephalic, 50 cm. in horizontal circumference; of normal configuration; the bones thin and containing a moderate amount of diploë. The dura mater was very tense, while in the longitudinal sinus were post-mortem clots and dark fluid blood. The inner meninges were thin and delicate throughout, moderately vascular and non-adherent. The right cerebral hemisphere was much more voluminous than the left, the cortex and inner meninges about the fissure of Rolando of a greenish colour, and presenting here distinct fluctuation. Incision over this area revealed an abscess about the size of a goose egg, filled with thick greenish tenacious pus, of a remarkably foetid odour. Around this main abscess were numerous smaller seats of suppuration, varying in size from a pea to a walnut, all containing pus of a similar character and each surrounded by a definite greyish-white capsule.

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Closer examination showed that the involved areas lay in the upper third of the ascending frontal and parietal convolutions and the posterior third of the middle and superior frontal, together with a part of the corona radiata. Numerous minute ecchymoses were seen in the cerebral substance about the abscesses. The basal ganglia were free from disease and were separated from the suppurating areas by white substance, 1 cm. in thickness. Otherwise the cerebrum, cerebellum, and medulla, as well as their vessels, were in all respects normal, except that the cerebral convolutions were somewhat flattened.

The oral cavity, pharynx, and larynx were pale; the tonsils and thyroid gland manifested no evidence of disease. The right lung at its lowest portion was firmly adherent, the overlying pleura markedly thickened and traversed by numerous sinuses. From section of this part the lung was seen to be converted into a dense thickened mass of fibrous tissue in which but little trace of alveolar arrangement remained; no nodules were discernible. Elsewhere in the organ there was no sign of disease, nor did the left lung present any abnormality beyond hyperæmia and a few areas of hypostatic congestion. Heart and pericardium normal.

Peribronchial lymph glands of the right side partially enlarged, and presenting numerous greyish-white areas. Abdomen had no abnormal contents. Liver normal. Spleen pale but not enlarged.

Kidneys were pale, somewhat large and friable; numerous isolated greyish-white areas of the size of hempseed were dotted over the surfaces of both organs. The remaining portion of the genito-urinary tract normal in every respect. Stomach and intestines presented no evidence of disease. Likewise the pancreas and adrenals.

Examination of fresh specimens of the pus from each of the cutaneous sinuses, as well as from the cerebral abscesses, showed yellowish granules in which the actinomyces were readily detected. Numerous and careful examinations, however, failed to reveal, in fresh specimens, any sign of the same germ in the contents of the ulcer situated about the alveolar process of the upper jaw.

PATHOLOGICAL ANATOMICAL DIAGNOSIS.—*Actinomyces pulmonis d. Actinomyces parietis thoracis. Abscessus actinomycetici metastatici cruris d., cerebri hemispherii d. et renum.*

Hardened specimens from affected portions of the right lung, brain, skin, and kidneys as well as from the tonsils and peribronchial lymph glands, and the diseased part of the upper jaw, were embedded in celloidin. From these, numerous sections were cut and stained with hæmatoxylin, as well as after Gram's method.

The sections from the lungs manifested conditions of both acute and advanced chronic inflammation. In the former case were seen numerous abscesses and tracts of suppuration in various portions of the lung tissue. The bronchi especially were affected, showing collections of leucocytes in their lumina as well as all about their walls, from which the epithelial lining had in great part disappeared. Directly in connection with these bronchi and bronchioles could be seen many of the above mentioned suppurating tracts, leading in various directions into the surrounding tissue. In numerous specimens, too, actinomyces were found directly in the lumen of a bronchus, whose epithelial lining was often readily seen. The parasites here were large, partially calcified, stained rather poorly, and showed numerous clubbed fibrils. The chronic inflammation, on the other hand, was manifested by advanced interstitial pneumonia,

the alveolar arrangement of the lung tissue being scarcely discernible; while in those areas, where the alveoli had retained their outline, their lumina were filled with small round cells, and the walls were greatly thickened. The presence of thickened arteries, and marked anthracosis was superadded. Specimens of the *brain* were examined both from the margin of the larger abscesses and from where the minuter seats of suppuration existed. The larger abscesses presented at their edges dense masses of small round cells closely packed together, and evidently in a stage of advanced degeneration. Around this area was a zone of concentrically arranged fibrous tissue of recent growth, which in most places gave a fairly definite boundary to the abscess, though in other parts the limitations were less distinctly defined, inasmuch as a moderately copious small cell infiltration invaded the surrounding cerebral tissue.

The cerebral vessels in the neighbourhood were somewhat thickened, dilated, and surrounded by a greater or less number of leucocytes. The actinomyces, in moderate quantity, were small, stained deeply, and existed only amid the dense masses of cells in the abscess margin. Sections from the brain, cut so as to include the minuter abscesses, presented, in these, collections of leucocytes surrounded by recently formed fibrous tissue with many nuclei. The surrounding cerebral substance was infiltrated with small round cells, and contained vessels filled with blood, around whose walls were numerous leucocytes. In no place, however, was there any evidence of true chronic inflammation. The actinomyces were here present in large numbers, and centrally situated in the abscesses. In all cases they stained well, the filaments being particularly distinct, and the clubbed ends in most cases wanting.

The *kidneys*, too, were examined, and the nature of the small greyish white areas more accurately determined. These in the form of minute multiple abscesses, chiefly in the cortex, existed in isolated patches, while the kidney substance presented otherwise merely a parenchymatous degeneration of its tubular epithelium and numerous casts. No general small-celled infiltration nor granulation tissue could be detected. The abscesses consisted merely of circumscribed masses of small round cells, containing in some instances giant cell formations. The invading parasite was likewise found in the centre of one of these abscesses in the immediate neighbourhood of a glomerulus, being in an early stage of development, composed chiefly of filaments, and manifesting but little evidence of clubbed formation.

The *skin*, examined by similar methods, showed in its sinuses numerous broken-down leucocytes, and the edges likewise infiltrated with pus cells. The walls of the sinuses contained more or less recent fibrous tissue, with small-celled infiltration, and the vessels of the neighbouring parts were hyperæmic, and surrounded by clusters of leucocytes. Here the actinomyces were found in moderate numbers among the broken-down pus cells within the sinuses, and their filaments showed with

marked clearness numerous clubbed endings. The *tonsils* and *peri-bronchial glands* contained no evidence of infection, while careful examination of sections of the ulcerated alveolar process showed, beyond various stages of osseous inflammation and caries of the dental root, no trace whatever of actinomycetes. Sections specially stained by Gram's method and with methylene-blue showed no evidence of other micro-organisms in any of the tissues examined. There too, however, in addition to the small leucocytes, were seen several giant cells, in most cases observed in the centre of a glomerulus, while the parasite was seen centrally situated in an abscess, immediately in juxtaposition to the capillary loops.

As regards the sinuses in the skin and subcutaneous tissue, those in the right leg are likewise undoubtedly metastatic, whereas all those in the side of the thorax and in the back, although also probably metastatic, cannot be positively regarded as such, inasmuch as their intimate topographical relationship to the diseased lung might render infection by continuity a possibility. The fact that no direct connection between the two processes could be found, does not exclude this means of infection, inasmuch as the parasite, in many instances, may penetrate extensive areas of tissue without a noticeable trace of its advance being left behind.

Finally, from the facts above given, one will observe the very marked resemblance of the disease in Case 1, to the tubercular process, inasmuch as here a distinctly atypical course was taken, viz., an involvement of the pulmonary apices. Its importance to the clinician may make it worthy of mention in view of the fact that J. Israel, in his remarks on differential diagnosis, regards the basal seat of the actinomycotic lesions as one of the main criteria in distinguishing that disease from tuberculosis.

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From the above data it will be apparent that an inquiry into the pathogenesis in these two cases presents no great difficulties, and that, in both instances, the nature of the process warrants their being placed under Group 2 of J. Israel's classification, namely, "primary actinomycosis of the lungs." In Case 1 the very chronic pulmonary inflammation with its extreme fibroid changes, especially in the left lung, where the conditions were more advanced, represents, without a doubt, the oldest pathological process in any of the organs. Further, the condition of the smaller bronchi, whose lumina filled with leucocytes were continuous with suppurating tracts, traceable to varying distances in the altered lung tissue, and in which the parasites were readily found, render it all the more certain that here the original invasion took place. Hence, the disease progressed *per continuitatem* towards the periphery, affecting the overlying pleura, and reaching the mediastinal tissue till it finally, after eroding the bones in its course, perforated the anterior thoracic wall. In the brain the lesions were undoubtedly metastatic in origin, arising

from invasion of the systemic circulation by the parasite. Microscopically, these metastases presented the ordinary appearances of abscesses.

The second case affords still more clearly a ready explanation of the parasite's invasion and progress within the body. That the disease was likewise pulmonary in origin is proved from the fact that, not only were actinomyces found in the suppurating tracts leading from the bronchi, but directly within the lumina themselves. Moreover, the extensive growth of interstitial tissue likewise points to the lungs as the seat of the oldest pathological affection. Invasion, then, of the lungs was succeeded by a markedly slow, chronic, and insidious process, to which no attention was drawn, till after a metastatic area had been discovered in a distant part of the body. Having, then, slowly progressed in the lung tissue, the disease was here propagated directly on to the overlying pleura, which likewise became chronically inflamed and formed dense adhesions. From the original seat of invasion, metastases, through the blood channels, invaded the brain and kidneys. Those in the brain presented features resembling very closely the conditions described in Case 1, there being but little granulation tissue present, and the main mass consisting of broken-down leucocytes, not differing therefore in general appearance from the usual form of pyæmic metastases.

By far the most recent process was seen in the kidneys, where, too, the connection of the infection with the circulatory system was evident.

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